UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/973,284	10/09/2001	Joy M. Campbell	P05273US0	5785

22885 7590 09/10/2002

MCKEE, VOORHEES & SEASE, P.L.C.
801 GRAND AVENUE
SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	8

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/973,284	CAMPBELL ET AL.	
	Examin r	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2002 and 01 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *9-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1- 8 and 16-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4&5* . 2/14/02 4/5/02
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-23 are pending.

2. Applicant's election with traverse of Group I, claims 1-8 and 16-23, filed on 5-1-02, is acknowledged.

Applicant's traversal is on the grounds that no separate search is required to search the non-elected groups as all claims are related as product and process of use and can be reviewed in a single. This is not found persuasive because MPEP 803(July 1998) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criterion and therefore establishes that serious burden is placed on the examiner by the examination Groups. The Inventions are distinct for reasons elaborated in the previous Office Action.

The requirement is still deemed proper and is therefore made FINAL.

Applicant elected chronic fatigue syndrome and blood as the species. Claims 1-2, 8, 16-17 and 23 read on the elected species.

Upon reconsideration, Examiner has extended the search to cover egg, milk, recombinant immunoglobulin expressed in a plant and recombinant immunoglobulin expressed in a bacteria recited in claims 3-7 and 18-22.

4. Claims 9-15 (non-elected Group II) are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

5. Claims 1-8, 16-23 are under examination as they read on a method of treating an aimal suffering from an immune dysfunction disease state associated with altered levels of IgG.

6. Applicant's IDS, filed 2-12-02 and 04-05-02 (Paper No. 4 and 5 respectively), is acknowledged. However, references B18-B20 and B23 were crossed out as they are duplicates of A12-A15, also references A9 and A10 were considered only in regard to the Abstract as the entire document was not found.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 6-8 and 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The "recombinant immunoglobulin" recited in claims 6-7 and 21-22 has no antecedent basis in base claims 1 and 16 respectively. Base claims 1 and 16 only recite an immunomodulating amount of immunoglobulin.

B. Claims 8 and 23 are indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of ..." with the use of the conjunction "and" rather than "or" in listing the species. See MPEP 706.03(Y).

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1- 8, 16-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating an animal suffering from chronic fatigue syndrome which associated with altered levels of IgG comprising administering to said animal immunoglobulin derived from blood, egg, milk, recombinant immunoglobulin expressed in a plant and recombinant immunoglobulin expressed in a bacteria does not reasonably provide enablement for a method for treating an animal suffering from any **immune dysfunction disease** state associated with altered levels IgG comprising administering to said animal an immunomodulating amount of immunoglobulin from an animal source in claims 1 and 16. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure does not enable one skilled in the art to practice the invention without any undue amount of experimentation.

At issue is whether or not the claimed method would function to treat any immune dysfunction disease such as " Kawasaki syndrome, asthma, rheumatoid arthritis, Crohn's disease, glaforsis host disease, human immunodeficiency virus, thrombocytopenia, anemia, nuetropenia, hemophilia, myasthenia gravis, multiple sclerosis, systemic lupus, demyelinating polyneurophathy, polymyositis and Sjogren's syndrome, insulin-dependent diabetes mellitus, bullous pemphiguoid, thyroid-related eye disease, ureitis and or any other disease state associated with altered IgG levels". The specification discloses significant decreases in specific antibody titers following primary and secondary rotavirus and PRRS vaccination. The exemplification is drawn to the effect of oral administration of plasma protein on antibody responses to primary and secondary rotavirus vaccination (page 30 of the specification).

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since no animals were used as model system to treat Kawasaki syndrome, asthma, rheumatoid arthritis, Crohn's disease, glaforsis host disease, human immunodeficiency virus, thrombocytopenia, anemia, nuetropenia, hemophilia, myasthenia gravis, multiple sclerosis, systemic lupus, demyelinating polyneurophathy, polymyositis and Sjogren's syndrome, insulin-dependent diabetes mellitus, bullous pemphiguoid, thyroid-related eye disease, ureitis and or any other disease state associated with altered IgG levels. It is not clear that reliance on data obtained from oral administration of plasma protein and its effect on antibody responses to primary and secondary rotavirus vaccination accurately reflects the relative mammal efficacy of the claimed therapeutic strategy. The specification does not adequately teach how to effectively treat any immune dysfunction disease or reach any therapeutic endpoint in mammals such as animals by administrating the immunoglobulin. The specification does not teach how to extrapolate data obtained from in the studies to the development of effective in vivo mammalian therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the pharmaceutical composition exemplified in the specification.

However, an effective protocol for the treatment for immune dysfunction diseases in animal is subject to a number of factors which enter the picture beyond simply the administration of the pharmaceutical composition in an acceptable formulation. Demonstrating significant decreases in specific antibody titers following primary and secondary rotavirus and PRRS vaccination cannot alone support the predictability of the method for treating said Kawasaki syndrome, asthma, rheumatoid arthritis, Crohn's disease, glaforsis host disease, human immunodeficiency virus, thrombocytopenia, anemia, nuetropenia, hemophilia, myasthenia gravis, multiple sclerosis, systemic lupus, demyelinating polyneurophathy, polymyositis and Sjogren's syndrome, insulin-dependent diabetes mellitus, bullous pemphiguoid, thyroid-related eye disease, ureitis and or any other disease state associated with altered IgG levels through administration of the immunomodulating amount of immunoglobulin. Van Noort et al. (International Review of Cytology, 1998) indicate factors that effect autoimmune disease such as genetic, environmental and hormonal (Page 176, Paragraph 3). The ability of a host to suppress

and thereby treat immune dysfunction disease will vary depending upon factors such as the condition of the host and burden of disease.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-2, 8 and 16-17 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Lloyd *et al* (Am J Med. 1990, 89:561-568) as is evidenced by INTRAGAM® Data Sheet.

The Lloyd *et al* teach a method of treating patients suffering from chronic fatigue syndrome that is characterized by IgG subclass deficiency (page 561, right column 3rd paragraph in particular) comprising administering to the patients an immunomodulating amount of immunoglobulin (INTRAGAM®) from an animal source (page 562, under Drug Formulation in particular). Lloyd *et al* further teach that immunoglobulin is administered by continuous infusion in dosage of 2g (IgG)/kg or placebo (10% w/v maltose) (page 562, under Drug Formulation in particular). Immunoglobulin in placebo is considered as composition.

Further, as is evidenced by INTRAGAM® Data Sheet that INTRAGAM® is made by a cold ethanol fractionation of large pools of human plasma obtained from voluntary blood donors (page 1, paragraph 2 in particular).

The reference teachings anticipate the claimed invention.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 3-4, 16 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lloyd *et al* (Am J Med. 1990, 89:561-568), as is evidenced by INTRAGAM® Data Sheet, in view of U.S patent No. 5,871,731.

The teachings of Lloyd *et al* reference have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that immunoglobulin from an animal source is blood and fractions thereof in claim 2, egg and fractions thereof in claims 3 and 18 and milk and fractions thereof in claims 4 and 19.

The `731 patent teaches the immunoglobulins can be prepared by known techniques from plasma, for example from eggs or from milk. Furthermore, the isolation of immunoglobulins from milk of immunized cows or from eggs from immunized hens is used to immunize pregnant women or mother animals against bacterial pathogens (column 3, lines 31-36 in particular). The `731 patent further teaches that the production of the immunoglobulins from plasma is relatively complicated and therefore very expensive, the immunoglobulins are preferably isolated from milk (column 2, lines 61-67 and column 3, lines 1-2 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the immunoglobulin from egg or from milk taught by the `731 patent with the immunoglobulin from blood in a method of treating an animal suffering from chronic fatigue syndrome taught by Lloyd *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because producing immunoglobulin from milk is easy and inexpensive and producing immunoglobulins from milk of immunized cows or from eggs from immunized hens is used to immunize pregnant women or mother animals against bacterial pathogens as taught by the `731 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 1, 5-6, 16 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lloyd *et al* (Am J Med. 1990, 89:561-568), as is evidenced by INTRAGAM® Data Sheet, in view of WO 96/21012 (1996).

The teachings of Lloyd *et al* reference have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the animal immunoglobulin is recombinant in claims 5 and 20 wherein the recombinant is expressed in a plant in claims 6 and 21.

The `012 publication teaches the production of large amounts immunoglobulins in plants with great efficiency and economical feasibility (see page 5 lines 31-35 in particular) using recombinant vector (see page 54 lines 34-35 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the immunoglobulin that is expressed in a plant using recombinant vector taught by the `102 publication with the immunoglobulin from blood in a method of treating an animal suffering from chronic fatigue syndrome taught by Lloyd *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because immunoglobulins expressed in plants have great efficiency and economical feasibility as taught by `012 publication.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. Claims 1, 5, 7, 16, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lloyd *et al* (Am J Med. 1990, 89:561-568), as is evidenced by INTRAGAM® Data Sheet, in view of U.S. Patent No. 5,348,867 (1994).

The teachings of Lloyd *et al* reference have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the animal immunoglobulin is recombinant in claims 5 and 20 wherein the recombinant is expressed in a bacteria in claims 7 and 22.

The `867 patent teaches recombinant immunoglobulins from bacteria. The `867 patent further teaches that the variety of recombinant immunoglobulins from bacteria is greater than the number of antibody molecules that can be generated by the mammalian cell (column 2, line 68 and column 3, lines 1-12 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the recombinant immunoglobulins that is expressed in a bacteria taught by the `867 publication with the immunoglobulin from blood in a method of treating an animal suffering from chronic fatigue syndrome taught by Lloyd *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the variety of recombinant immunoglobulins from bacteria is greater than the number of antibody molecules that can be generated by the mammalian cell as taught by `867 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
September 9, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600